IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

VYTACERA BIO, LLC,

Plaintiff,

v.

CYTOMX THERAPEUTICS, INC.,

Defendant.

C.A. No. 20-333-GBW-CJB

[redacted]

DEFENDANT CYTOMX THERAPEUTICS, INC.'S REPLY BRIEF IN SUPPORT OF ITS RULE 12(c) MOTION FOR JUDGMENT ON THE PLEADINGS

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I. INTRODUCTION

Following claim construction, there is a gaping hole at the center of Vytacera's case that warrants judgment in CytomX's favor now, on the pleadings. Based on the Court's *Markman* ruling, Vytacera has no literal infringement argument against CytomX's Probody therapeutics, the *only* accused product in the Complaint. Vytacera does not dispute this. And, as demonstrated again below, any doctrine of equivalents ("DOE") theory is too implausible to move forward; nothing in Vytacera's opposition shows otherwise.

Vytacera's pivot position—a new infringement theory premised on a supposed [redacted] serving as the claimed "inhibitor"—cannot salvage Vytacera's case. First, the theory is nowhere found in Vytacera's Complaint. Vytacera concedes this by relying on a host of extraneous evidence to try to substantiate this new theory without once citing the Complaint in support. *See* D.I. 168 at 4-10. Vytacera also ignores that a [redacted] cannot infringe because it is *never administered*, nor is it deactivatable in proximity to target cells, as required by the claims. Compounding matters, the documents Vytacera improperly relies on establish that the newly accused [redacted], and thus outside the reach of U.S. patent laws.

The Court should reject Vytacera's last-ditch attempt to keep its case alive and grant CytomX's Motion.

II. JUDGMENT SHOULD BE ENTERED THAT CYTOMX'S PROBODY THERAPEUTICS DO NOT INFRINGE

A. Vytacera Does Not Dispute that Judgment of No Literal Infringement by CytomX's Probody Therapeutics Should Be Entered

Vytacera does not dispute a central premise of CytomX's Motion: that Probody therapeutics—the fully-formed proteins for administration to patients—do not literally infringe the '504 and '913 patents, meaning judgment of no literal infringement should be entered. As set

forth in Plaintiffs' opening brief, a Probody therapeutic does not meet the claims' "inhibitor" limitation. In construing "inhibitor" as "a molecule, separate from the [BAA/antibody] . . .," the Court held that "the inhibitor and the BAA must always be separate molecules." D.I. 130 at 6-8. A Probody therapeutic, which Vytacera's Complaint accuses of infringement, is unquestionably a single molecule. D.I. 165 at 7-11. Because there is no dispute that a fully formed Probody therapeutic cannot literally meet the Court's "inhibitor" construction, the Court should grant judgment on the pleadings of no literal infringement of all claims of the '504 and '913 patents for CytomX's Probody therapeutics.

B. Under the Court's Claim Construction, There Is No Plausible DOE Theory Against Probody Therapeutics, So Judgment Should Follow

Vytacera's newly lodged DOE theory against Probody therapeutics should be disposed of on the pleadings, too. As an initial matter, it is found nowhere in Vytacera's Complaint; indeed, all Vytacera does is point to a rote recitation of the words "doctrine of equivalents." More still, Vytacera's DOE theory based on purported equivalence between CytomX's Probody therapeutics (wherein the alleged inhibitor and BAA are *not separate*) and the claimed inhibitor (which the Court has mandated *must be separate* from the BAA), is not plausible and is thus inadequate to survive a motion for judgment on the pleadings. *See Ashcroft v. Iqbal*, 556 U.S. 662, 678 (2009) ("plausibility standard" requires more than a "sheer possibility"); *Bibbs v. Trans Union LLC*, 43 F.4th 331, 339 (3d Cir. 2022) (applying plausible pleading standard to 12(c) motion).

Specifically, it is not plausible that the differences between CytomX's Probody therapeutics and the claimed inhibitor are insubstantial. *See Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 812 (Fed. Cir. 2002) ("An element in the accused product is equivalent to a claim limitation if the differences between the two are 'insubstantial' to [a

POSITA].”). In construing “inhibitor,” this Court has already recognized that single molecules containing both an alleged inhibitor and BAA, such as CytomX’s Probody therapeutics, are *substantially different* from the claimed inhibitors. As the Court held, “the inhibitor and the BAA must always be separate molecules” in part because the “inhibitor” must “take[] an action – for example, binding, inhibiting, or suppressing – that affects the BAA.” D.I. 155 at 2. In view of that required functionality, the Court further explained, “[i]t is hard to conceive of how a first entity (the inhibitor) could be said to ‘inhibit’ … a second entity (the biologically active agent), if those two things were actually all part of the same chemical molecule.” *Id.* at 2-3 (quoting D.I. 130 at 7). And the Court even went so far as to say “it seems nonsensical that the inhibitor could be part of the same molecule of the very thing that it inhibits.” D.I. 130 at 7.

Vytacera’s argument that the claims may be infringed by a single-molecule inhibitor/BAA that the Court has characterized as inconceivable and nonsensical is the epitome of a position that is not plausible and that cannot save it from judgment on the pleadings. DOE is not a silver bullet allowing a party to propel past the pleadings regardless of how strained its argument may be. *See Amgen Inc. v. Sandoz Inc.*, 923 F.3d 1023, 1029 (Fed. Cir. 2019), *as modified on reh’g*, 776 F. App’x 707 (Fed. Cir. 2019) (“The doctrine of equivalents is not simply the second prong of every infringement charge, regularly available to extend protection beyond the scope of the claims.” (quotation marks omitted)). The numerous limitations on the doctrine, such as the rule against claim vitiation, reflect this. *Trading Techs. Int’l, Inc. v. eSpeed, Inc.*, 595 F.3d 1340, 1355 (Fed. Cir. 2010) (“Claim vitiation applies when there is a clear, substantial difference or a difference in kind between the claim limitation and the accused product.” (quotation marks omitted)). And, where a DOE argument, considered in view of those limitations, is not plausible on the pleadings (either due to claim vitiation issues or general

implausibility regarding insubstantial differences), no authority suggests the case must continue. *See Cumberland Pharms. Inc. v. Sagent Agila LLC*, No. 12-cv-825-LPS, 2013 WL 5913742, at *3 (D. Del. Nov. 1, 2013) (dismissing DOE argument due to vitiation issues apparent on the pleadings).

Further, Vytacera's cursory, eleventh-hour function-way-result (FWR) analysis applies the wrong inquiry for this art. In the context of therapeutics, the correct DOE analysis focuses on the limitations of the claims (which here would be, e.g., the first and second moieties of the inhibitor) and asks whether the accused product contains an equivalent for each limitation such that the therapeutic as a whole can be considered insubstantially different. *See Mylan Institutional LLC v. Aurobindo Pharma Ltd.*, 857 F.3d 858, 866-70 (Fed. Cir. 2017) (explaining that compounds with biological uses are ill-suited for FWR because, for example, the test can be manipulated to frame drugs with markedly different structures (e.g. aspirin and ibuprofen) as equivalents). As the court observed in *Mylan*, and as would be the case here, application of FWR, as opposed to the insubstantiality of the differences test, can lead to the absurd and incorrect result of dramatically different molecules being deemed equivalent. *Id.*

Vytacera's DOE argument also runs afoul of the most basic principles of the DOE analysis. As the Supreme Court has specified, "the doctrine of equivalents must be applied to individual elements of the claim, not to the invention as a whole." *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 29 (1997). Vytacera's FWR theory (found nowhere in the Complaint) relies on generalizations between the alleged overall similarity of the claimed inhibitor (*separate from* a BAA) and Probody therapeutics (wherein the alleged inhibitor and BAA *are not separate*). *See* D.I. 168 at 14-15 (arguing that Probody therapeutics are the same as "the claimed invention" without discussing specific claim limitations). By generalizing about

overall similarity, Vytacera's theory misses the question at the core of the FWR analysis: whether the differences between a *specific claim limitation* and a *specific structure* in an accused device could plausibly be considered insubstantial.

Vytacera's DOE position, articulated for the first time in opposition, is not plausible, applies the wrong analytical framework, and is inconsistent with the Court's *Markman* decision. The Court should grant CytomX's Motion as to DOE for the accused Probody therapeutics.

III. JUDGMENT SHOULD BE ENTERED IN CYTOMX'S FAVOR ON THE NEWLY ALLEGED [redacted]

Recognizing it cannot sustain its original infringement theory, Vytacera's opposition pivots to a highly speculative—and wholly unpled—theory that accuses an alleged [redacted] not a Probody therapeutic, of infringement. D.I. 168 at 4-10. This theory cannot salvage Vytacera's case, so judgment should be entered for CytomX.

A. Vytacera's Pleadings Do Not Accuse the Newly Alleged [redacted]

Vytacera's Complaint does not allege that the newly alleged [redacted] infringes. Far from showing the Court where in its Complaint it pled facts plausible to sustain its new infringement theory, Vytacera does not even cite to its Complaint until the *penultimate paragraph* of its brief. *See* D.I. 168 at 18. And even then, Vytacera provides nothing more than a generic recitation that the Complaint "adequately pleads infringement both literally and under [DOE] by showing how CytomX's Probodies infringe each and every claim limitation of the independent claims of the Patents-in-Suit." *Id.* (citing D.I. 1 at ¶¶ 89-95, 142-150). But what Vytacera pled has *nothing* to do with any [redacted] (let alone the alleged

[redacted] Vytacera now accuses[1]); Vytacera's allegations are limited to the fully formed, single-molecule Probody therapeutic, where the alleged inhibitor is unequivocally attached to the BAA/antibody. *See* D.I. 165 at 8-11 (collecting Complaint evidence showing Probody is a single molecule).

That Vytacera claims in opposition to have either adequately or plausibly pled infringement by a [redacted] that is quasi-separate is not credible. As Vytacera itself points out, on a Rule 12(c) motion, the Court "must accept as true all factual allegations in the complaint[.]" D.I. 168 at 1. The factual allegations in Vytacera's Complaint speak for themselves; no [redacted] is ever even hinted at.

Instead, to present its new infringement theory, Vytacera deviates entirely from the Complaint, extensively invoking a CytomX Investigational New Drug (IND) Application and previously uncited scientific literature. But this is improper. Only a "document integral to or explicitly relied upon in the complaint" can be considered in resolving a motion for judgment on the pleadings. *In re Burlington Coat Factory Sec. Litig.*, 114 F.3d 1410, 1426 (3d Cir. 1997).

What is more, the Complaint makes clear that CytomX's IND is ***not*** "integral" as Vytacera cursorily argues, and so should not be considered in deciding this Motion. In fact, Vytacera carefully pled infringement ***to avoid accusing anything in*** CytomX's IND because such activities are protected from infringement by the "safe harbor" of 35 U.S.C. § 271(e)(1). *See* D.I. 1 at ¶¶ 55, 64, 65. The Complaint discusses the safe harbor extensively, and even cites *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 207 (2005), the seminal case which holds that activities that produce data for submission in an IND ***are not infringement***. D.I. 1 at

[1] CytomX disagrees that the [redacted] Regardless, the Court need not reach that issue to grant CytomX's Motion; Vytacera never pled this theory.

¶¶ 50-53. So, far from citing the IND or suggesting it is "integral" to the Complaint, Vytacera carefully and unmistakably alleged infringement separate and apart from the IND. Simply put, CytomX's IND is not part of, and cannot save, the Complaint.[2]

The additional scientific articles Vytacera uses in its effort to backfill are even further afield. *See* D.I. 168 at 4-10. And while Vytacera does rely on one exhibit that appears in its Complaint, (D.I. 169, Ex. C), Vytacera never suggests that article demonstrates the plausibility of its [redacted] theory. Vytacera only relies on the article to show the (undisputed) structure and function of the final Probody therapeutic, and not the newly-accused [redacted]

In sum, Vytacera does not argue (let alone demonstrate) that its Complaint, standing alone, plausibly alleges its [redacted] infringement theory. And Vytacera's numerous extraneous exhibits put forward to substantiate that new theory cannot be considered in deciding CytomX's Motion. Vytacera's new [redacted] infringement theory thus cannot and should not prevent the Court from granting CytomX's Motion.[3]

[2] *AstraZeneca Pharms. LP v. Apotex Corp.*, 669 F.3d 1370, 1378 (Fed. Cir. 2012) does not suggest otherwise. In that Hatch-Waxman case, the ANDA was central to the complaint because its filing constituted the actionable act of infringement. *See* 35 U.S.C. § 271(e)(2). It thus was reasonable to consider the ANDA to resolve the case on the pleadings. *Id.* at 1378 n.5. Not so here. Vytacera's Complaint is *not* based on CytomX's IND or any other safe harbor-protected activity. The Court should thus decline to consider the IND in resolving CytomX's Motion.

[3] Vytacera's cited cases denying Rule 12(c) motions are inapposite. Two cases were denied because they hinged on claim construction that had not yet occurred—the opposite of the facts here. *Barrier1 Sys. v. RSA Protective Techs., LLC*, C.A. No. 1:20-cv-00340, 2021 U.S. Dist. LEXIS 193823, at **7-8 (D. Del. Oct. 7, 2021); *Novartis Pharms. Corp. v. Actavis, Inc.*, C.A. No. 1:12-cv-00366, 2012 U.S. Dist. LEXIS 176445, at **17, 34 (D. Del. Dec. 5, 2012). And in the other two cases, direct infringement was not at issue. *Align Tech, Inc. v. 3Shape A/S*, C.A. No. 1:17-cv-1647, 2020 U.S. Dist. LEXIS 187445, at *4 (D. Del. Oct. 8, 2020); *3Shape A/S v. Align Tech., Inc.*, C.A. No. 1:18-cv-0886, 2019 U.S. Dist. LEXIS 53510, at **8-9 (D. Del. Mar. 29, 2019). None control here.

B. Judgment of Non-Infringement Is Warranted Under Vytacera's New Theory

But even if Vytacera had properly pled its new [redacted] infringement theory—and it did not—judgment of non-infringement of the patents-in-suit is proper. Simply put, the [redacted] cannot possibly meet the limitations of the claims.

All claims of the '913 patent require "a method of site specific activation…comprising ***administration of an inhibitor***[.]" The '913 claims also require the inhibitor to be "administered alone or together with said antibody," which the Court construed to mean the "inhibitor is administered by itself, i.e., not with said antibody, or [the] inhibitor is co-administered with said antibody." D.I. 130 at 10-11; *see also* D.I. 155 at 6 (the Court agreeing with Judge Burke's analysis). Thus, administration must be shown to prove infringement of the '913 patent.

Here, it is undisputed that, should Vytacera's alleged [redacted] exist at all, it exists only [redacted], and is neither administrable, nor ever administered. *See* D.I. 168 at 7-8 (describing [redacted]); *id.* at 10 ("Accordingly, [redacted]); *see also id.* at 8 ("Thus, [redacted]). Notably, Vytacera's opposition does not even attempt to show how the alleged [redacted] meets the "administration" step of the '913 patent; it clearly cannot.

The '504 patent claims also contain a requirement that the claimed inhibitor must be in an administrable state, which squarely places the alleged [redacted] outside their scope. According to the claims, the inhibitor must be "deactivatable by a reagent produced by a target cell[.]" Because it will never be administered, the alleged [redacted]

[redacted] cannot meet this limitation. *See* D.I. 168 at 7-8 ([redacted]). Indeed, it defies reason that a [redacted] that is never isolated as an administrable product (let alone is actually administered) would ever come into close proximity with a target cell and be deactivated, as the claims require.

Vytacera's Complaint readily admits that the accused inhibitor must be administrable and deactivatable at a target cell. It describes the asserted patents as covering technology that "assists with the delivery of biologics compounds to specific cells," (D.I. 1 at ¶ 17), and more specifically as relating to "inhibitors suppressing the biological activity of administered agents, which might have undesirable systemic effects, until they are in the proximity of targeted cells," (*id*. at ¶ 18). This is why the Complaint's infringement allegations focus solely on CytomX's Probody therapeutics—while they do not contain the required inhibitor as demonstrated previously and again above, they are at least intended to be administered. *Id*. at ¶¶ 89-113. Simply put, the claimed inhibitors are active and functional in the targeted microenvironment found within the body. The alleged [redacted] is not, as Vytacera concedes, so cannot be the claimed "inhibitor."

Finally, the CytomX IND Vytacera improperly relies upon demonstrates [redacted] (outside the United States). *See* Ex. A (stating that [redacted]). Under federal patent law, direct infringement can only occur when someone "makes, uses, offers to sell, or sells any patented invention, ***within the United States*** or imports ***into the United States*** any patented invention…" 35 U.S.C. § 271(a) (emphasis added). Because U.S. patent laws do not have extraterritorial effect, CytomX cannot be found to infringe the claims of either patent-in-suit since the accused [redacted]

[redacted] is never even in the United States according to the IND Vytacera invokes to support its theory. *Microsoft Corp. v. AT & T Corp.*, 550 U.S. 437, 454-55 (2007).

Thus, the Court should grant CytomX's Motion with respect to infringement of the alleged [redacted] for all claims of the '913 and '504 patents if the Court considers the [redacted] accused within the Complaint.

IV. CONCLUSION

For the foregoing reasons, CytomX respectfully requests that the Court grant CytomX's Motion and enter judgment of non-infringement in CytomX's favor.

Dated: November 4, 2022

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that a true and correct copy of the above and foregoing document has been served on November 4, 2022, to all counsel of record who are deemed to have consented to electronic service via the Court's CM/ECF system.

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